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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/942,320	08/29/2001	Kamal D. Mehta	D6351	7732

7590

05/09/2003

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EXAMINER
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MONSHIPOURI, MARYAM

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 05/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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**Office Action Summary**Application No.  
**09/942,320**Applicant(s)  
**Mehta et al.**Examiner  
**Maryam Monshipouri**Art Unit  
**1652****-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --****Period for Reply**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above, claim(s) 4-6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_                      6) ☐ Other:

Art Unit: 1652

Applicant's response to restriction requirement filed 3/3/2003 (Paper # 5) is acknowledged. Applicant elected Group I directed to claims 1-3 without traverse. Claims 4-6 are withdrawn as drawn to no-elected invention.

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inducing low density lipoprotein (LDL) receptor expression comprising contacting HepG2 cells with TPA or anisomycin, does not reasonably provide enablement for methods of inducing LDL receptor expression comprising contacting any cell with a compound that activates P42/44 MAPK, wherein activation of said kinase results in the induction of LDL receptor expression.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

Art Unit: 1652

The specification does not teach about the kind of cells that have LDL receptors and p42/44 MAPK simultaneously, which can be exploited for such method. No examples of such cells are provided either. Current state of the art indicates that many bacterial cells or even mammalian cells do not have LDL receptors or p42/44 MAPK machinery simultaneously, in order to be used in such method.

Therefore due to lack of sufficient teachings and examples provided in the specification and due unpredictability in the prior art as to which kind of cells are likely to be effectively utilized in claimed method one of skill in the art has to go through the burden of undue experimentation in order to screen for those cells that can be used in current method and as such the claims go beyond the scope of the disclosure.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Kumar et al. (J. Lipid Research, 38, 2240-2248, 1997). Kumar teaches a method of treating HepG2 cells with MAPK/ERK pathway inducer (which includes p42/44MAPK inducer), 12-O-

Art Unit: 1652

tetradecanoylphorbol -13 acetate (TPA), wherein the mRNA levels of LDL receptor have increased by 20-fold due to said treatment (see figure 5 and page 2244). Even though Kumar does not explicitly teach that the induction of LDL receptor is independent of cell growth regulation, its TPA induction of LDL receptor inherently occurs: independently of cell growth regulation and due to sole P42/44 MAPK activation, anticipating claims 1-2.

Kumar shows that treating HepG2 cells with MEK inhibitor, PD98509, blocks TPA-mediated LDL receptor mRNA induction, in a dose dependent manner. Said teaching implies that LDL receptor expression is dependent on p42/44MAPK activation, as said activation "in vivo" occurs by MEK, anticipating claim 3.

5. Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by Dhawan et al. (J. Lipid Research, 40, 1911-1919, Oct 1999). Dhawan teaches a method of treatment of HepG2 cells with ansiomycin (an activator of p42/44 MAPK pathway), which resulted in enhanced expression levels of LDL receptor (see figure 1). Dhawan teaches that ansiomycin activation is due solely to activation of p42/44 MAPK, anticipating claims 1 and 3.

Even though Dhawan does not explicitly teach that the induction of LDL receptor is independent of cell growth regulation, its ansiomycin induction of LDL receptor inherently occurs independently of cell growth regulation, anticipating claim 2.

6. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Dhawan et al. (FASEB J., 13(4), part 1, pp.A194, March 1999). Dhawan teaches that in HepG2 hepatic cells activation of p42/44 MAPK (which inherently occurs by addition of activators) is sufficient to

Art Unit: 1652

induce full LDL receptor expression in the absence of cytokines, anticipating claims 1 and 3. Even though Dhawan does not explicitly teach that LDL receptor expression occurs independently of cell growth regulation said phenomenon inherently occurs in HepG2 derived cell line of Dhawan, when treated with P42/44 activators, anticipating claim 2.

**No claims are allowed.**

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Maryam Monshipouri, Ph.D. whose telephone number is (703) 308-1083.

The Examiner can normally be reached daily from 8:30 A.M. to 5:00 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. P. Achutamurthy, can be reached at (703) 308-3804. The OFFICIAL fax number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

  
**MARYAM MONSHIPOURI, PH.D.**  
**PRIMARY EXAMINER**